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 EP 0223978 A1

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 Online databases: WPI AND CLAIMS

**(54) Blood typing**

(57) A method and device for typing human blood groups is provided based on red blood cell agglutination. Reagents specific to various blood groups are placed into localized areas on a filter-type medium which is pervious to red blood cells. The blood to be typed is applied to each of the areas and the medium is subjected to a lateral flow of wash fluid. Red blood cells agglutinated by a specific reagent are retained in the medium producing a visually distinguishable area. When the red blood cells are not agglutinated, they are washed out of the medium with the wash fluid. Reagents are e.g. mono or polyclonal antibodies specific to blood groups of the ABO and Rhesus systems.

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Fig. 1

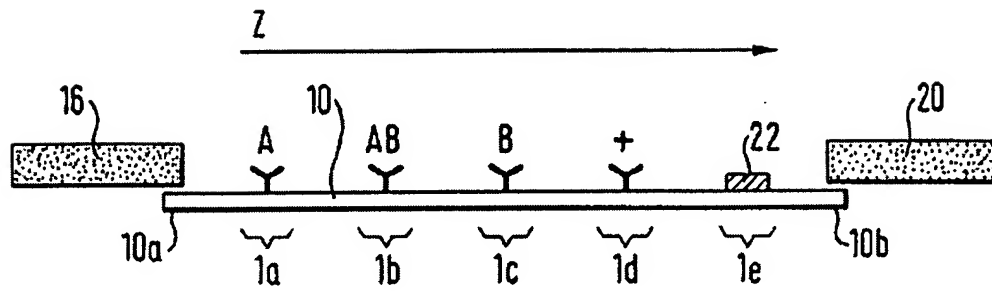


Fig. 2

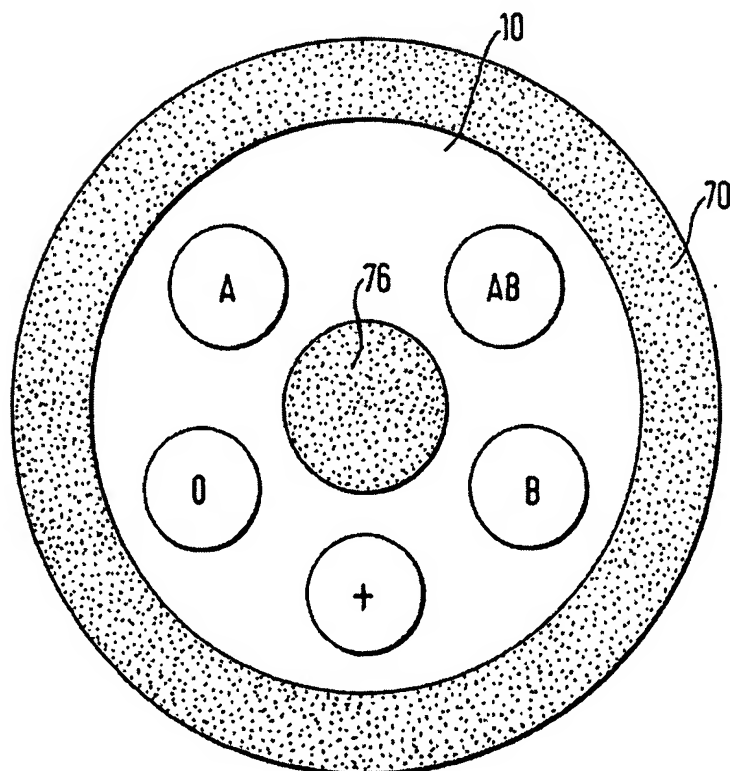


Fig. 3

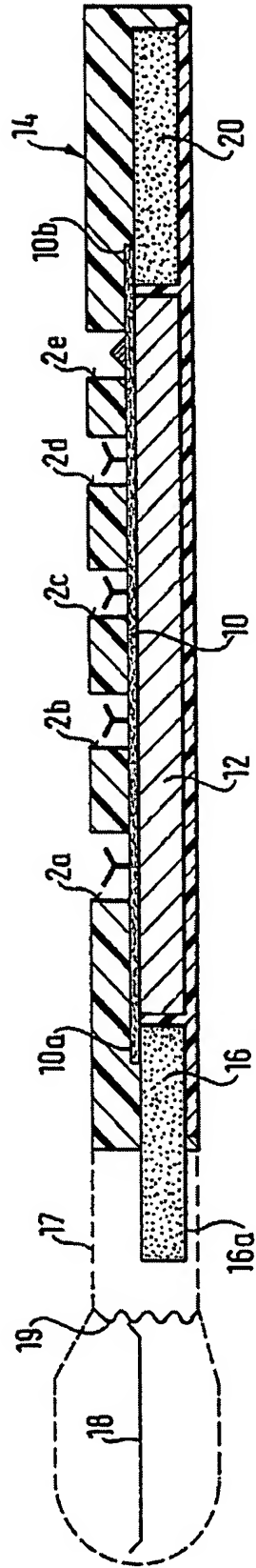
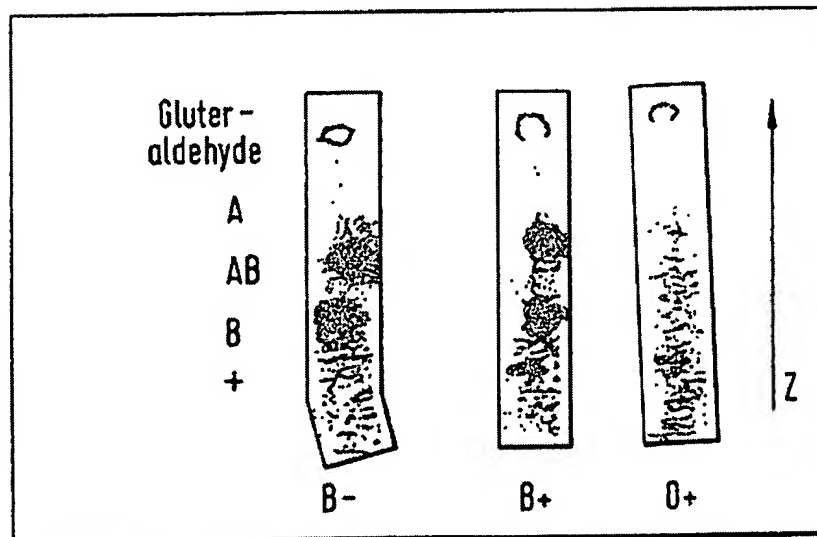


Fig. 4



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## A method and device for typing human blood groups

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15 The present invention relates to a method and a device for typing human blood groups by determining the presence or absence of specific antigens and antibodies in a blood sample through antibody-antigen complex formation detected by red blood cell agglutination.

20 Human blood is classified into a number of systems of groups and various groups within these systems can be identified by the presence or absence of specific antigens. Under the ABO system red cell antigens and antibodies are specified in accordance with the following table.

25

Phenotype	Genotype	Antigens	Naturally-Occurring Antibodies	Frequency (UK) %
30 O	OO	O	Anti-A,B	46
A	AA or AO	A	Anti-B	42
B	BB or BO	B	Anti-A	9
AB	AB	AB	None	3

35

In the Rhesus system, the red blood cells of the ABO blood groups most frequently found can be classified into those containing antigen D and those containing no antigen D (Rhesus positive versus Rhesus negative). When transfusing blood, knowing the blood group of the person donating blood and the  
40 person receiving the transfusion is of vital importance.

Conventional blood group typing involves visual or microscopic observation of the agglutination of red cells. Although reliable, agglutination reactions suffer from the disadvantages of subjective interpretation, the need for washed red blood cells  
5 and the need for refrigerated reagents and a centrifuge.

A dipstick for determining ABO blood groups is disclosed by Plapp et al. in "The Lancet", June 28, 1986, pages 1465-1466. The dipsticks are prepared by binding murine monoclonal anti-A or anti-B to nitrocellulose or nylon membranes. After  
10 applying whole blood to the surface of the membrane, unbound red cells are washed out by swirling the dipstick back and forth in a beaker of saline. This method has the disadvantage of requiring a separate beaker of saline solution and in addition the excessive washing caused by the swirling of the dipstick does not lead to reliable and easy to interpret results.

15 Other methods rely on the availability of a central laboratory with the appropriate facilities. It will be appreciated that many situations arise in medical treatment, in which the blood group of a patient must be known on site, however where no central laboratory is immediately available.

20 It is therefore the object of the present invention to provide a rapid and reliable method of determination of blood groups and an associated device, which can be employed on site only with the addition of a blood sample and which is also simple and inexpensive.

25 In accordance with the present invention a method and a device for typing blood groups are provided as defined in the claims. According to the present method, reagents, preferably antibodies specific to various blood groups are placed into localized areas on a thin section of a filter-type medium, preferably a fibrous  
30 material which is pervious to red blood cells. The blood to be typed is applied to each of the areas and the medium is then subjected to a lateral flow of wash fluid through the areas. Red blood cells agglutinated by a specific reagent in a given area are retained in the medium producing a coloured area, thus indicating a positive result. When red blood cells are not agglutinated in a given area, the  
35 medium is such that the unagglutinated red blood cells are washed out with the wash fluid leaving an uncoloured region on the medium. This negative result is

an indication that the antigen for a specific blood group was not present on the red blood cells.

To be operable, the medium employed in the method must be pervious to red  
5 blood cells in the unagglutinated state, i.e. under application of the wash fluid the red blood cells can laterally migrate away from the localized areas when no antibody-antigen complex formation has taken place.

In a preferred embodiment, the medium comprises fibrous hydrophilic material, in  
10 particular polyethylene fibers which have been made hydrophilic through suitable treatment. Preferably the fibers are formed from a composition of LLDPE (linear low-density polyethylene) and a wetting agent. The most preferred LLDPE is an ethylene/octene copolymer as described in US 4 578 414.

15 The device according to the present invention comprises a piece of filter-type material, preferably fibrous material having a plurality of localized areas arranged therein, where the areas contain reagents specific to various blood groups and wherein the material is substantially pervious to red blood cells and substantially  
20 impervious to agglutinated red blood cells. The material is also pervious to a wash fluid which is capable of washing essentially all unagglutinated red blood cells out of a respective area.

In one preferred embodiment of the device, the filter-type material is a fibrous hydrophilic material located on a non-absorbent or hydrophobic support means.  
25 The fibrous material and support means are enclosed in a housing. The housing is provided with openings to expose the areas containing reagents, thus allowing the application of the blood to be typed. In a further embodiment, the piece of fibrous material is provided as an elongated strip. The device is also provided with supply means on a first end for introducing the wash solution and absorbing  
30 means on the other end of the strip for enhancing the flow or wicking of wash solution across the medium. The agglutination results according to the present invention can be readily read by visual inspection. The positive results indicated by coloured spots in the localized area for a particular blood group are highly distinguishable over the areas where no complex formation has taken place and  
35 the red blood cells have been washed out.

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The blood group test can be completed within about 3 minutes, so that the result is not only easy to read but is also readily available. The device can be hand-held and in one embodiment is provided with prestored wash fluid. It then forms a self-contained unit which only requires the application of a blood sample.

5

The blood to be typed can be fresh blood used immediately prior to clotting, blood preserved using heparin or SAG-M. The blood need not be centrifuged or pretreated prior to testing.

10 The device has the further advantage that it is enclosed in a housing in a manner which minimizes exposure to the blood by the user. After the test, the device can be disposed of with minimal hazard and potentially no human contact of the blood.

15 Further details of the invention will become apparent in the following description of embodiments by way of reference to the drawings.

Figure 1 shows a schematic diagram representing the basic principles of the present invention.

20

Figure 2 shows an embodiment employing a circular piece of fibrous material in a device according to the present invention.

25

Figure 3 shows a further embodiment of the device according to the present invention.

Figure 4 shows examples of blood typing tests obtained according to the present invention.

30 The invention is broadly applicable to the use of blood typing reagents, in particular antibodies specific to the antigens on red blood cells of human blood. In the embodiment of Fig. 1, the antibodies anti-A, anti-AB and anti-B are placed in the localized areas or zones 1a, 1b and 1c. The areas can have any shape, a circular or dot-shape is preferred. An anti-Rhesus D-positive antibody is placed in  
35 the area 1d in Fig. 1 while the area 1e contains a non-specific binding agent for



red blood cells as a control. Any suitable combination or sequence of antibodies can be used as will be discussed further below.

The employed antibodies can be monoclonal or polyclonal antibodies specific to the blood groups of the ABO and Rhesus systems. Preferred antibodies are murine monoclonal or polyclonal antibodies for example obtainable from Lorne Laboratories Ltd., Great Britain.

The antibodies are spot loaded in liquid form to the medium 10 of Fig. 1. Any suitable means can be employed for applying the antibodies, for example by hand or using a thin layer chromatography applicator. For each localized zone 1a-1d a volume of 1 to 10  $\mu$ l of antibody is applied. Preferably the antibody is applied in an amount of 2 to 5  $\mu$ l for each localized zone. In one embodiment, a binding agent for all red blood cells is provided at one end of the medium 10 namely in the zone 1e. The binding agent can be applied in an amount of 1 to 10  $\mu$ l. Preferred agents are gluteraldehyde and lectins.

After application of the antibodies and optionally a binding agent, the medium is dried by heating for 30 minutes to 2 hours at a temperature in the range of 30°C to 60°C. For this purpose, the medium can be placed on a non-absorbent surface in order that antibody not be extracted from the medium. It has been found that particularly good results are obtained when heating is carried out in the preferred range of 30 minutes to 1 hour in a temperature range of 30°C to 40°C.

The result of this heating is that the antibodies are dried onto or deposited upon the filter type material surface. This can be the outer and/or inner surface, preferably the outer and inner surfaces of the material.

The filter type material can also be provided with a backing. The backing if employed should be non-absorbent, preferably of a plastic material which can be bound to the filter-type material. Possible methods of binding include adhesive bonding, heat or ultrasonic welding (continuous or intermittent) or casting or forming the material directly onto a backing. Most preferably, the filter-type material is a hydrophilic fibrous material with a backing of a hydrophobic media such as polytetrafluoroethylene (PTFE) or polyvinylidene fluoride (PVDF) as well as nonporous films such as polyolefin sheet or fibrous web.

The material 10 according to the present invention is a filter-type material capable of being loaded with antibodies as described above. The dried-on antibodies are retained by the material when kept under dry conditions. The material has the  
5 further property that it is permeable to red blood cells, i.e. the pore size in the medium is such that red blood cells are not retained to a significant extent and also do not bind to the fibrous material. On the other hand, agglutinated red blood cell complexes are retained by the material, i.e. cannot to a significant extent migrate through the material.

10 The material in a particular embodiment can be a polyolefin, preferably polyethylene, polypropylene or an ethylene-lower olefin copolymer. LLDPE (linear low density polyethylene) is most preferred. Generally suitable polymers include those of olefins of 2 to 10 C atoms. More preferred is a copolymer of ethylene and  
15 0.5 to 8 weight % of a comonomer, more preferably 1 to 7 weight %. Preferred comonomers are olefins with 4 to 10 C atoms, most preferably 4 to 8 C atoms, most preferred is a copolymer of ethylene and 1-octene.

When polyethylene is used, it is made water wettable or hydrophilic by the  
20 addition of a suitable amount of a wetting or surface active agent. Wetting agents can include

- a) an alkoxyated alkyl phenol along with a mixed mono-, di- and/or triglyceride or
- 25 b) a polyoxyalkylene fatty acid ester or
- c) a combination of (b) and any part of (a).

Such wetting agents are described in US 4,578,414. The alkoxyated alkyl phenol is preferably one where the alkyl group has 1 to 20 carbon atoms, most preferably  
30 about 6 to about 12 carbon atoms. A polyethoxy chain is the preferred polyalkoxy chain. The mixed glyceride is preferably a glyceride of a fatty acid. The fatty acid may be saturated or unsaturated and is preferably a mixture of fatty acids having a carbon chain length in the range of about 12 to about 18 carbon atoms. Particularly preferred wetting agents include Atmer 645, a complex mixed glyceride  
35 with a long chain fatty acid adduct, available from ICI America Inc. Another

wetting agent is a monoester of Z-9-octadecenoic acid and 1, 2, 3 -propanetriol, available from Dow Chemical as XU 61518.10.

The above described substances can be processed to form the filter type material of the present invention by any suitable method. The preferred fibrous hydrophilic material can be made for example from fibers, preferably from spun fiber, particularly from melt spun fibers. The most preferred form of the present material is one produced by melt blowing the above mentioned preferred ethylene copolymer combined with a wetting agent.

The formed fibrous material can be in the form of a web or mat and can be calendered. Uncalendered material has been found more effective however and is preferred.

The preferred fibrous hydrophilic material according to the present invention has one or more of the following properties in combination in the following broad or preferred ranges.

Property	broad range	preferred range
Wetting agent content (% by weight) in the poly- ethylene composition	0.5 - 5.0	0.6 - 3.0 particularly about 1.0
Fiber diameter ( $\mu\text{m}$ )	1.0 - 15	2 - 11
CWST of the melt blown fiber (dynes/cm)	30 - 120	100 - 120
Pore size of the fiber material (microns) (ASTM F 316-80)	3 - 300	5 - 20
Retained water volume/ Volume of material ( $\text{cm}^3$ water/ $\text{cm}^3$ material)	0.6 - 0.95	0.7 - 0.9

particularly about 0.85

Material weight (g/ft <sup>2</sup> )	2 - 8	3 - 4
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5 Treatment

(calendered or uncalendered)	-	uncalendered preferred
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Thickness (cm)	0.01 - 0.07	0.02 - 0.06
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10 particularly about 0.03

For the purposes of the embodiments in figures 1 and 2, the material is provided in elongated strips, for example 6 cm long and 1 cm wide.

15 Having prepared a strip 10 of the fibrous hydrophilic material as shown in Fig. 1, an amount of the blood to be typed is applied to each of the localized zones 1, preferably about one drop of blood or approximately 5 to 10  $\mu$ l. The reaction of the antibodies in the medium with the added blood is immediate and there is no need to allow a longer time for complex formation before proceeding to the  
20 washing step. On the other hand, it has been found that the blood can be left on the spots or zones up to 6 minutes before introducing the wash solution. This did not impair the test results.

A wash fluid or solution is then introduced into the medium, for example at a  
25 first end 10a as shown in the embodiment of Fig. 1. The solution can be introduced by any suitable means. Figure 1 shows a feed pad 16 which for example could be preloaded with wash solution and squeezed to emit the solution. For the above mentioned embodiment with a strip size of 6 by 1 cm, it has been found that a volume of about 0.5 ml of wash solution is optimal. Suitable wash  
30 solutions include phosphate-buffered saline (PBS), physiological saline or deionized water.

After introducing the wash solution, it wicks along the strip 10 in the flow direction indicated with the arrow Z under capillary action. The solution is left  
35 to wick along the medium carrying with it unagglutinated blood cells. The solution and cells migrate to the opposite end of the strip shown in Fig. 1 as the second

end 10b. In a preferred embodiment, an absorbent pad 20 is provided in contact with the second end of the strip, thereby enhancing the wicking action. According to Fig. 1, the wash solution flows in a longitudinal direction and sequentially through the respective zones 1. The invention however is not limited to this configuration. The wash solution could for example be introduced to flow laterally with respect to the strip indicated in Fig. 1. It is also possible that the piece of fibrous material used as the medium be provided in a round, oval, square or any other shape with any appropriate configuration of the zones containing antibody.

10 Good results have been found according to the present invention, where the reagent-loaded areas have a diameter of about 0.2 to about 0.8 cm, preferably 0.25 to 0.5 cm. The lateral or longitudinal flow of wash solution then guarantees a clearly distinguishable positive or negative result. It is therefore preferred to provide the flow of wash solution in the plane of the material, whether this be  
15 longitudinally, transversely or for example radially when the medium is provided in a round shape.

A second embodiment employing a circular piece of the fibrous material is shown in Fig. 2. The wash fluid is introduced by means of the feed pad 76 and flows  
20 outwardly through the antibody containing zones. In this embodiment, an absorbent pad 70 is provided about the circumference of the fibrous material 10, again having the function of enhancing migration through the material.

The purpose of the wash solution is to remove red blood cells from those zones  
25 or areas where the red blood cells have not been agglutinated by the associated antibody. As mentioned above, the medium is pervious to red blood cells and they migrate out of a given zone where antibody-antigen complex formation has not taken place and leave behind an uncoloured region, i.e. the color of the area returns substantially to its initial color.

30 A zone in which agglutination has taken place retains a coloured spot, normally red, and indicates a positive result. Antibody-antigen reactions have produced an agglutination complex which is retained in the medium. The formed complexes in the medium are retained in the pores and cannot migrate through the medium  
35 with the wash solution.

Having carried out the test which generally will require approximately 3 minutes, the blood group type can be read according to the presence or absence of red spots. For example with the antibodies employed in the embodiment of figure 1, a positive reaction for the zones A and AB and a negative result for the zones B and Rh+ would indicate the blood group A-. The blood group O- for example would be indicated by no reaction in any of the zones A, AB, B or Rh+. This example demonstrates the purpose of the red cell binding agent 22 in the zone 1e. For the group O- all red blood cells wash out of the regions containing anti-B, anti-AB, anti-B and Rh+ leaving uncoloured zones. The presence of a red spot in the zone 1e for the binding agent is a control for the fact that red blood cells have indeed passed through the previously mentioned zones and reached the second end 10b of the medium in Fig. 1. Thus they migrate from the zones 1a to 1d and are captured at 1e by the binding agent 22.

An embodiment of the device according to the present invention is illustrated in Fig. 3. The device comprises a piece of fibrous material 10 mounted on a non-absorbent substrate layer 12. Alternatively the fibrous material 10 can be provided with a non-absorbent backing which would relinquish the need for a substrate layer. Such a backing for example can be a hydrophobic resin, preferably a hydrophobic polyolefin layer bonded to the fibrous material. The fibrous material 10 and support means 12 are enclosed in a housing 14 which preferably consists of a synthetic material such as plastic. The support means 12 can either be a separate material or preferably part of the plastic housing. In the embodiment of Fig. 3, the antibody containing zones on the piece of fibrous material are located adjacently along a longitudinal axis of said material where the piece of fibrous material is preferably an elongated strip. The housing comprises a plurality of openings or wells 2 which expose the antibody containing zones and allow application of the blood to be typed.

The device of the present invention is also provided with supply means 16, 17 and 18 for introducing wash solution to a first end 10a of the fibrous material. In one embodiment, the supply means comprise a feed pad 16 in contact with the end 10a of the fibrous material where the feed pad 16 has an exposed portion 16a into which the wash solution can be supplied. This can be accomplished for example by manually applying the wash solution in the appropriate amount to the exposed end portion. According to Fig. 3, the supply means can also be comprised of a bulb 18 containing the wash solution, where a breakable seal

connects the contents of the bulb through a passage 17 to the feed pad 16. Exerting pressure on the bulb 18 breaks the seal 19 and allow a flow of wash solution to the pad 16 and subsequently through the strip of fibrous material 10.

5 The device according to the invention is also provided with absorbing means 20 arranged in contact with the second end 10b of the strip of fibrous material. As mentioned above, the absorption of the wash solution at the end of the strip promotes flow by wicking to said second end and therefore through the antibody containing zones. The absorbing means 20 are preferably completely enclosed in  
10 the housing which reduces the possibility of blood contact with the user of the device during and after the test.

The wells 2 or windows are also arranged as recesses which will also prevent direct contact with the blood being typed. The results of the test can be easily  
15 read by observing the presence or absence of read spots in the respective windows.

The performance of the method is illustrated by the following example.

#### 20 Example

This example illustrates the present method for testing the blood groups B-, B+ and O+ under various conditions. In a first run, 2  $\mu$ l of the antibody anti-A, anti-AB and anti-B and anti-Rh+, were applied to a fibrous hydrophilic polyethylene  
25 medium. The fibrous material was prepared from a copolymer of 94 weight % ethylene and 6 weight % octene-1, a copolymer available commercially from Dow Chemical Company as Aspun 6809. To this copolymer was added 1 weight-% of a monoester of Z-9-octadecenoic acid and 1, 2, 3 - propanetriol as the wetting agent. The mixture was blended in a Banbury mixer for 30 minutes. The mixture  
30 was then turned into a homogenous blend by passage through an extruder at a temperature just above the melting point of the thermoplastic polymer at about 205°C. The extrudate was then cooled and chopped into pellets. The pellets were then heated to 610°F (231°C) and fiberized by passing through a melt blowing die at 150 psi resin pressure and 20 psi air pressure. The emerging fibers were  
35 collected to form a fibrous web of 4 g/ft<sup>2</sup> for use as the medium. The antibody was soaked into the medium and was dried in an oven for 30 minutes at 37°C.

Three such strips of material 6 by 1 cm were prepared for testing the three blood groups B-, B+ and O+. Same-day blood in an amount of 2  $\mu$ l was applied to each antibody containing zone. After applying the blood, the material was immediately wicked with 0.5 ml of phosphate-buffered saline. The results are given  
5 in Fig. 4. The presence of the blood group B+ is indicated by the (red) spots at the zones B and AB, while the Rhesus factor Rh+ is indicated by the (red) spot at the zone for the Rh+ antibody. The B-test shows coloration in the zones B and AB, with no reaction in the Rh zone. The blood group O+ shows a clear, colorless region in the zones for the antibodies A, AB and B and a mark  
10 indicating the Rh+ factor.

Gluteraldehyde was used as a positive control in an additional zone. The positive control can be seen by the (red) spots at the top of the strips along the flow direction Z.



# CLAIMS

- 5 1. A method for typing blood groups comprising
  - a) adding an amount of blood to a plurality of areas of a thin section of a filter-type material,
  - aa) wherein different reagents which are capable of agglutinating red blood cells in a way specific to the blood type are located in  
10 individual areas of the material,
  - bb) wherein said filter type material is substantially pervious to red blood cells and substantially impervious to agglutinated red blood cells, and is pervious to a wash fluid which is capable of washing essentially all non-agglutinated red blood cells out of a respective area,
  - 15 b) passing through said section such a wash fluid in a direction substantially orthogonal to the thickness dimension of said section and removing substantially all non-agglutinated red blood cells out of the respective areas while leaving significant amounts of agglutinated red blood cells in other respective areas, thereby producing coloured and  
20 uncoloured areas on said section.
2. Method of claim 1, characterized in that said filter-type material has a further area having a non-specific binding agent for red blood cells located therein, in particular wherein said binding agent is selected from gluteraldehyde and  
25 lectin.
3. Method of claim 1 or 2, characterized in that said reagents are antibodies specific to the antigens of the blood groups of the ABO and Rhesus systems, in particular wherein said reagents are murine monoclonal or polyclonal  
30 antibodies.
4. Method of claim 3, characterized in that antibodies specific to the antigens of the ABO blood groups A, AB and B and the Rhesus group D positive are located in said areas of the filter-type material.

5. Method of one of the preceding claims, characterized in that said wash fluid is selected from the group of phosphate-buffered saline, physiological saline and deionized water.
- 5 6. Method of one of the preceding claims, characterized in that said filter-type material comprises fibrous hydrophilic material.
7. Method of claim 6, characterized in that said fibrous hydrophilic material is polyethylene fiber containing a wetting agent.
- 10 8. Method of claim 6 or 7, characterized in that said fibrous hydrophilic material has a pore size of about 5 to about 20 microns, and a ratio of retained water volume to volume of material of about 0.7 to about 0.9 cm<sup>3</sup> water/cm<sup>3</sup> material.
- 15 9. Method of one of the preceding claims, characterized in that said filter-type material is provided as an elongated strip with said areas arranged along a longitudinal axis thereof.
- 20 10. Method of claim 9, characterized in that said wash fluid is introduced at a first end of said elongated strip and flows longitudinally through each of said areas to a second end of said elongated strip, said wash fluid transporting with it non-agglutinated red blood cells.
- 25 11. Method of claim 9 or 10, characterized in that said non-specific binding agent is located in the wash flow direction from said first strip end to said second strip end following said antibody-containing zones but before said second end.
12. Method of claim 9 to 13, characterized in that an absorbent pad is provided  
30 at said second end of said elongated strip to enhance the flow of wash fluid and non-agglutinated red blood cells in the direction of the second end.
13. Method of preparing a filter-type material for use in the blood typing method of the claims 1 to 12, characterized in that blood-group specific antibodies are  
35 attached to localized areas on said material by applying a volume of antibody

in the range of 1 to 10  $\mu$ l to the respective areas and heating for 30 min. to 2 hours at a temperature in the range of 30°C to 60°C.

14. Method of claim 13, characterized in that a volume in the range of 2 to 5  $\mu$ l of antibody is applied to said localized zones.
15. Method of claim 13 or 14, characterized in that said heating is carried out for 30 min. to 1 hour at a temperature in the range of 30°C to 40°C.
16. Method of any of the claims 13 to 15, characterized in that said filter-type material comprises fibrous hydrophilic material.
17. Method of claim 16, characterized in that said fibrous hydrophilic material is polyethylene fiber containing a wetting agent, in particular wherein said wetting agent is selected from the group of
  - a) an alkoxylated alkyl phenol along with a mixed mono-, di- and/or tri-glyceride or
  - b) a polyoxyalkylene fatty acid ester or
  - c) a combination of (b) and any part of (a).
18. Method of claims 16 or 17, characterized in that said fibrous hydrophilic material has a pore size of about 5 to 20 microns and a ratio of retained water volume to volume of material of about 0.7 to about 0.9  $\text{cm}^3$  water/ $\text{cm}^3$  material.
19. Device for typing blood groups comprising a piece (10) of filter-type, preferably fibrous material having a plurality of localized areas (1) arranged therein, said areas containing reagents specific to various blood groups, wherein said material is substantially pervious to red blood cells and substantially impervious to agglutinated red blood cells, and is pervious to a wash fluid which is capable of washing essentially all non-agglutinated red blood cells out of a respective area.
20. Device of claim 19, further characterized by
  - a) a housing (14) enclosing said piece of filter-type material and a nonabsorbent support means (12) upon which said piece is located, said

- housing having openings (2) to expose said reagent containing areas, to allow application of the blood to be typed,
- b) supply means (16, 17, 18) for introducing a wash fluid to a first end (10a) of said piece of filter-type material, said supply means having an exposed portion (16a) in said housing,
- 5 (c) absorbing means (20) enclosed within said housing and in contact with a second end (10b) of said piece of filter-type material to enhance the flow of said wash fluid.
- 10 21. Device of claim 19 or 20, characterized in that said piece (10) of filter-type material comprises a further localized area (1e) containing a non-specific binding agent for red blood cells and an opening (2e) in said housing to expose said further localized area.
- 15 22. Device of claim 19 or 21, characterized in that said reagents are antibodies specific to the antigens of the blood groups of the ABO and Rhesus systems, in particular wherein said reagents are murine monoclonal or polyclonal antibodies.
- 20 23. Device of claim 22, characterized in that localized areas (1) are provided for antibodies specific to the antigens of the blood groups A, AB and B and the Rhesus group D positive.
24. Device of any of the claims 19 to 23, characterized in that said piece of  
25 filter-type material is an elongated strip (10) of fibrous hydrophilic material having a thickness of 1 to 4 mm.
25. Device of claim 24, characterized in that said fibrous hydrophilic material comprises polyethylene fiber containing a wetting agent, in particular wherein  
30 said wetting agent is selected from the group of
- a) an alkoxyated alkyl phenol along with a mixed mono-, di- and/or tri-glyceride or
- b) a polyoxyalkylene fatty acid ester or
- c) a combination of (b) and any part of (a).

26. Device of claim 25, characterized in that said fibrous material has a pore size of 5 to 20 microns and a ratio of retained water volume to volume of material of about 0.7 to about 0.9 cm<sup>3</sup> water/cm<sup>3</sup> material.
- 5 27. Device of any of the claims 24 to 26, characterized in that said absorbing means (20) comprise an absorbent pad in overlapping contact with said second end (10b) of the elongated strip.
- 10 28. Device of any of the claims 24 to 27, characterized in that said supply means comprise a feed pad (16) with an exposed end (16a), which is arranged so that the feed pad can be externally wetted at the exposed end to supply a wash fluid to the first end (10a) of the elongated strip.
- 15 29. Device of any of the claims 24 to 27, characterized in that supply means comprise a feed pad (16) and a bulb (18) containing said wash fluid, where one wall of said bulb (18) is provided with a breakable seal (19), which when broken allows communication of said wash fluid to said feed pad (16).

**Patents Act 1977**  
**Examiner's report to the Comptroller under**  
**Section 17 (The Search Report)**

Application number  
  
9025733.8

**Relevant Technical fields**

(i) UK Cl (Edition K ) G1B (BBD, BCB)

(ii) Int Cl (Edition 5 ) G01N

**Databases (see over)**

(i) UK Patent Office

(ii) ONLINE DATABASES: WPI AND CLAIMS

**Search Examiner**

M R WENDT

**Date of Search**

9 JANUARY 1992

Documents considered relevant following a search in respect of claims

1-26

Category (see over)	Identity of document and relevant passages	Relevant to claim(s)
X	EP A1 0223978 (ABBOTT) eg see Abstract, page 5 lines 24-38, page 6 line 9 and 21 page 9 lines 52 etc claims	1,3,4-6, 19,22,23 at least

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